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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**National Institutes of Health**

**Government-Owned Inventions; Availability for Licensing**

**AGENCY:** National Institutes of Health, HHS.

**ACTION:** Notice.

**SUMMARY:** The invention listed below is owned by an agency of the U.S. Government and is available for licensing to achieve expeditious commercialization of results of federally-funded research and development. Foreign patent applications are filed on selected inventions to extend market coverage for companies and may also be available for licensing.

**FOR FURTHER INFORMATION CONTACT:** Dr. Maryann Puglielli at (240)-627-3723, or *maryann.puglielli@nih.gov.* Licensing information may be obtained by communicating with the Technology Transfer and Intellectual Property Office, National Institute of Allergy and Infectious Diseases, 5601 Fishers Lane, Rockville, MD 20852: tel. 301-496-2644. A signed Confidential Disclosure Agreement will be required to receive copies of unpublished information related to the invention.

**SUPPLEMENTARY INFORMATION:** Technology description follows:

**Replicating RNA Vaccine For Crimean-Congo Hemorrhagic Fever Virus.**

**Description of Technology:**

Crimean-Congo hemorrhagic fever (CCHF) is a deadly hemorrhagic fever having a high mortality rate. The disease results from infection of an individual by Crimean-Congo hemorrhagic fever virus (CCHFV), which is a tick-borne bunyavirus endemic in Southern and Eastern Europe, Africa, the Middle East, and Asia. Geographically, case distribution is consistent with the range of *Hyalomma* genus ticks, the main reservoir of CCHFV, and is likely to expand due to climate change. Humans may be infected from tick bites, through contact with infected animals or animal tissue. Nosocomial human-to-human transmission has also been described primarily for healthcare workers. Initial symptoms of CCHF include acute onset of a non-specific febrile illness consisting of sudden fever, myalgia, diarrhea, nausea, and vomiting. The hemorrhagic phase is characterized by large areas of severe bruising and uncontrolled bleeding throughout the body; among hospitalized patients, case fatality rates have ranged from 9-50%. Currently, there is no approved specific antiviral or vaccine for CCHFV infection.

Scientists at NIAID in collaboration with HDT Bio have developed a replicating RNA (repRNA) vaccine based on Venezuelan Equine Encephalitis Virus replicon RNA expressing either the nucleoprotein (repNP) or the glycoprotein precursor (repGPC) from CCHFV alone or in combination. In mice, the repNP vaccine primarily elicited a robust but non-neutralizing antibody response while repGPC elicited primarily cellular immunity against epitopes in the CCHFV NSm and Gc proteins. Vaccination with repNP or repNP + repGPC resulted in protection against challenge with a heterologous strain of CCHFV in mice.

This technology is available for licensing for commercial development in accordance with 35 U.S.C. § 209 and 37 CFR Part 404, as well as for further development and evaluation under a research collaboration.

**Potential Commercial Applications:**

- Prophylactic usage against CCHFV infections in normal or high-risk populations

- Therapeutic treatment, alone or in combination, in patients with CCHFV infection
- Assay development for surveillance, diagnostic, and prevention measures

**Competitive Advantages:**

- Uses a cell-free system to express antigens thereby increasing safety of the vaccine.
- RepRNA as a platform can drive high-level protein expression and mimics viral replication in a single round of replication resulting in a more robust immune response in comparison to DNA and mRNA platforms.

**Development Stage:** Pre-clinical.

**Inventors:** Heinz Feldmann (NIAID); David Hawman, (NIAID); and Jesse Erasmus (HDT Bio)

**Publications:** Leventhal, S. et al., "Replicating RNA Vaccination Elicits an Unexpected Immune Response that Efficiently Protects Mice Against Lethal Crimean-Congo Hemorrhagic Fever Virus Challenge", EBioMedicine 82:104188 (2022).

**Intellectual Property:** U.S. provisional patent application 63/365,015 filed May 19, 2022

**Licensing Contact:** To license this technology, please contact Dr. Maryann Puglielli at (240)-627-3723, or *maryann.puglielli@nih.gov,* and reference E-103-2022.

**Collaborative Research Opportunity**: The National Institute of Allergy and Infectious Diseases is seeking statements of capability or interest from parties interested in collaborative research to further develop, evaluate, or commercialize this technology. For collaboration opportunities, please contact Dr. Maryann Puglielli at (240)-627-3723, or *maryann.puglielli@nih.gov.*

Date: February 8, 2023.

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[FR Doc. 2023-03595 Filed: 2/21/2023 8:45 am; Publication Date:  2/22/2023]